PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08.06.2004
Applicant's or agent's file reference: RLL-248WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB 03/01223	03.04.2003	03.04.2002

Applicant
RANBAXY LABORATORIES LIMITED et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
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ENTERED

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RLL-248WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/01223	International filing date *(day/month/year)* 03.04.2003	Priority date *(day/month/year)* 03.04.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/00, A61K9/00		
Applicant RANBAXY LABORATORIES LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.11.2003	08.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Rankin, R Telephone No. +31 70 340-4659

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/01223

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-12 as originally filed

Claims, Numbers

1-39 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1, 35-39

   because:

   ☒ the said international application, or the said claims Nos. 35-39 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☒ the claims, or said claims Nos. 1, 35 are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4, 5, 8, 9, 11, 14-21, 23-34, 38, 39
	No:	Claims	1-3, 6, 7, 10, 12, 13, 22, 35-37
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-39
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	35-39

2. Citations and explanations

   see separate sheet

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: Derwent WPI; AN: 1997-221685(JP(A) 9067247)
D2: Derwent WPI; AN: 1993-348367(JP(A) 5255120)
D3: Pz Prisma, Vi Verlag, Eschborn,, Go (2002), 9(3), 183-190
D4: WO-A-0048607
D5: WO-A-0217885

Regarding Medical Use Claims

Claims 35-39 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i) PCT)

For the assessment of the present claims 35-39 on the question whether they are industrially applicable, no unified criteria exist within the PCT Contracting States. The patentability can also be denendent upon the the formulation of the claims. The EPO, for example, does not recognise as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but may allow, however, the use of such a compound for the manufacture of a medicament for a new medical treatment.

Regarding A Lack of Essential Features

It is clear from the description on page 2, lines 26 & 27, page 3, lines 23 to line 27 and the examples to that the following features are essential to the definition of the invention:

Micronized Clarithromycin combined with rate controlling polymers and other excipients, wet mixed, granulated, dried and compressed into the form of a tablet.

Since independent claim 1 does not contain all of these features it does not meet the requirement of clarity following from Article 6 PCT.

Furthermore, since not all features essential to the solving of the technical problem posed are present in claim 1, claim 1 does not solve this problem with the consequence that claim 1 is not inventive (Article 33(3) PCT)

Regarding a Lack of Support

Article 6 PCT states that the claims should be clear, concise and fully supported by the description. Independent claims 1 and 35 are not supported by the description as required by Article 6 PCT. The scope of claims 1 and 35 is broader than justified

by the description and drawings. The reasons therefor are the following:
The application deals with the manufacture of pharmaceutical tablets containing clarithromycin. The problem addressed concerns the provision of tablets containing clarithromycin in a form suitable for once daily administration to a patient. This problem is solved by the applicant by micronizing clarithromycin, combining the drug with release-rate limiting polymers and other excipients, wet granulating the mixture, drying it and then compacting the granulate into tablet form.
As they stand, claims 1 and 35 could be directed towards producing any pharmaceutical composition containing micronized clarithromycin such as mouth washes, eye drops, lotions, creams etc etc.
As there is no support in the description for any of these other possible compositions which would fall under the wording of claims 1 and 35, said claims do not meet the requirements of Article 6 PCT as their scope is broader than justified by the description and drawings.

Regarding Novelty
The present application does not meet the requirements of Article 33(2) PCT, because the subject-matter of claims 1-3, 6, 7, 10, 12, 13, 22, 35-37 is not new.

The document D1 discloses (cf. Abstract):
Particles of clarithromycin ground to particles having size of 1-20 microns in a jet mill, mixed with a cellulose-derived polymer and granulated.
The subject-matter of claims 1-3, 6, 7, 10, 12, 13, 22, 35-37 is therefore not new (Article 33(2) PCT).

The document D2 discloses (cf. Abstract):
Particles of clarithromycin having a size of 2 microns are added to an aqueous polymer mixture to prepare a homogenous suspension of the drug which was subsequently processed to form particles.
The subject-matter of claims 1-3, 6, 7, 10, 12, 13, 22, 35-37 is therefore not new (Article 33(2) PCT).

Regarding Inventive Step
The problem to be solved in the present application is the provision of pharmaceutical tablets of clarithromycin which are suitable for once daily administration to a patient.
The solution of the present application resides in the micronization of clarithromycin, combining the drug with release-rate limiting polymers and other excipients, wet

granulating the mixture drying it and then compacting the granulate into tablet form.
As mentioned above, claim 1 of the present application does not solve the problem posed by the application since the features essential to solving said problem are not contained in claim 1. For this reason, claim 1 is inherently not inventive (Article 33(3) PCT)
The present application is not inventive with respect to documents D1 nd D2 since the subject matter contained in these documents renders claim 1 not novel and hence the present application is not inventive with respect to these documents (Article 33(3) PCT).

D4 and D5 address the same technical problem posed by the present application, namely the provision of a once-daily tablet formulation of clarithromycin.
As such, the problem is known in the art and the applicant has sought to find an alternate solution to this problem.

D4 (cf page 1, line 13 to page 2, line 7; examples) discloses clarithromycin embedded in a matrix containing cellulose derivatives, PVP and other excipients.

D5 (cf (page 1, lines 1-8; page 2, lines 9-12; examples) describes tablets of clarithromycin produced by combining sieved clarithromycin with rate controlling polymers such as cross-lined povidone, sodium alginate and xanthan gum; wet granulation of the mixture, drying of the granules and compressing the granules into a tables to yield a once-a-day tablet of clarithromycin.
D5 therefore represents the closest prior art.

The difference between the application and D5 is that the application employs micronized clarithromycin.

There is no technical effect of this difference since the products of D5 and the present application serve the same purpose.

The problem is therefore to provide an alternate clarithromycin tablet form for once-daily use.

The solution as provided by the applicant, ie using micronized clarithromycin is not inventive since this technique is common in the art and the skilled person would view it as a feasible alternative when faced with the problem posed, particularly in view of documents D1 and D2. Consequently, claims 28 to 34 are not inventive

(Article 33(3) PCT).